SCIENTIFIC ABSTRACT

The purpose of this study is to determine whether CD34+ cells from umbilical cord blood or bone marrow of infants/children with X-linked severe combined immunodeficiency (X-SCID) can be transduced by retroviral-mediated transfer of the normal human common gamma c common chain receptor (γc) cDNA, safely infused intravenously, resulting in the engraftment and production of mature peripheral blood leukocytes containing and expressing the γc cDNA. Potentially, the development of T lymphocytes expressing γc could restore functional immunity.

The study is open to infants diagnosed *in utero* / or children with X-SCID who are not candidates for HLA-Identical sibling donor bone marrow transplantation. Umbilical cord blood / bone marrow will be collected at parturition / during childhood and CD34+ cells will be isolated. The CD34+ cells will be transduced with the MND-γc retroviral vector. Transduction will be augmented with recombinant thrombopoietin, Stem Cell Factor and flt-3 ligand, using recombinant fibronectin CH-296 as a support matrix. After transduction, the cells will be washed thoroughly and infused intravenously into their donors without prior cytoreductive therapy. Infants and children will be started or maintained, respectively, on antibiotic prophylaxis and intravenous immunoglobulin therapy as standards of care prescribe.

Serial samples of peripheral blood will be analyzed for the frequency of cells containing the inserted γc vector. Expression of γc cDNA will be analyzed by FACS analysis (CRIM - subjects) and RT-PCR (both CRIM- and CRIM+ subjects). If persistent production of cells containing and expressing the γc gene is achieved, the end-point analyses for the frequency and function of transduced lymphocytes will be done.

In all, these studies will seek to determine the safety and efficacy of common gamma chain receptor (γc) gene transfer into autologous umbilical cord blood / bone marrow CD34+ cells to provide functional immunity.